Macrochelation, Cyclometallation and G-Quartet Formation: N^3- and C^8-Bound Pd^{II} Complexes of Adenine and Guanine

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Abstract: The reactions of Pd^{II} ions with a series of chelate-tethered derivatives of adenine and guanine have been studied and reveal a difference in the reactivity of the purine bases. Reactions of $[PdCl_2(MeCN)_2]$ and A-alkyl-enH · Cl (alkyl = propyl or ethyl, A = adenine, en = ethylenediamine) yield the monocationic species $[PdCl(A\text{-}N3\text{-}Et\text{-}en)]^+$ (**1**) and $[PdCl(A\text{-}N3\text{-}Pr\text{-}en)]^+$ (**2**). Both involve co-ordination at the minor groove site N3 of the nucleobase as confirmed by single-crystal X-ray analysis. Reactions with the analogous G-alkyl-enH · Cl derivatives (G = guanine, alkyl = ethyl or propyl) were more complex with a mixture of species being observed. For G-Et-en · HCl a product was isolated which was identified as $[PdCl(G\text{-}C8\text{-}Et\text{-}en)]^+$ (**3**). This compound contains a biomolecular metal–carbon bond involving C8 of the purine base. Crystallography of a product obtained from reaction of G-Pr-enH · Cl and $[Pd(MeCN)_4][NO_3]_2$ reveals an octacationic tetrameric complex (**4**), in which each ligand acts to bridge two metal ions through a combination of a tridentate binding mode involving the diamine and N3 and monodentate coordination at N7.

Keywords: adenine · cyclometalation · guanine · G-quartets · hydrogen bonding · palladium

Introduction

An insight into the interactions which take place between metal ions and nucleobases, nucleotides and nucleic acids is fundamental to the understanding of many biological phenomena. Hence such studies have become central to bioinorganic chemistry.[1–3] A key objective in this area has been to establish the details of these interactions. For the nucleobases, delineation of the preferred coordination sites has largely been facilitated by using simple model systems, particularly 9-alkylpurines and 1-alkylpyrimidines.[1–3] For purines these sites are now acknowledged as being N7 and N1, which, in double-stranded DNA (ds-DNA), are located in the major groove and at the helix centre respectively.

In contrast, while it is well established that organic reagents react with the minor groove site, N3[4] and the major groove site, C8[5] of purine nucleobases, the interaction of metal ions at these sites is not widely considered. An increasing number of reports, however, indicate that metal ions do bind at these less common sites with potentially significant effects.[6–14] For example, metal complexes are known to bind to the minor groove of ds-DNA,[11] divalent metal ions have been implicated in stabilizing A-tract structures through such interactions,[9] and individual nucleoside–phosphates have also been reported to interact with N3 in the cases of several divalent metal ions.[6]

Nucleobases can also react to form organometallic species as a result of metal–carbon bond formation. Early studies on the synthesis of tagged-nucleic acid demonstrated that nucleotide–triphosphates, UTP, CTP, dUTP and dCTP undergo mercuration at C5.[13] Guanosine and adenosine were also later confirmed to form metal–carbon-bonded derivatives through metallation at C8.[14] Transition metal ions have also been shown to form such organometallic species on reaction with nucleobases, though, in general these are restricted to examples with pyrimidines.[15]

We have recently begun to explore the reactivity of chelate-tethered nucleobase derivatives towards metal ions.[12, 16] Examples of mononuclear complexes involving either N3– or C8–metal binding have been observed with adenine.[12] Furthermore, the capacity for these ligands to bridge metal ions has led to the generation of discrete or extended polynuclear complexes.[16] These studies have also highlighted

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a base-specific interaction of the minor groove site of N3 with copper ions.[16] Here we report on the reactions of Pd^{II} ions with adenine and guanine derivatives tethered with ethylenediamine (en). The results highlight a significant difference in the reactivity of the two nucleobases. For adenine, the metal ion binds at the minor-groove based site of N3 in each case. With guanine, however, a mixture of products is observed, from which we have been able to isolate and characterise a C8-cyclometallated species for the G-Et-en derivative and a molecular-square which features both N3 and N7 coordination to the guanine moiety from reactions with G-Pr-en.

Results and Discussion

Reactions of Pd^{II} and adenine derivatives: Reactions of the adenine-derived ligands, A- Et-en and A-Pr-en, with Pd^{II} ions involved adding an aqueous solution of ligand as the hydrochloride salt to a refluxing solution of $PdCl_2$ in MeCN. Each reaction yielded a yellow solid upon work-up which analysed as $[PdCl(A\text{-}N3\text{-Et-en})]^+$ (**1**) or $[PdCl(A\text{-}N3\text{-Pr-en})]^+$ (**2**), as Cl^- salts. In the case of **1** conversion to the corresponding BF_4^- salt by metathesis with $NaBF_4$ was performed as an aid in the preparation of single crystals.

The molecular structures of **1** and **2** are shown in Figure 1 and Figure 2, respectively. In both complexes the palladium, co-ordinated by three nitrogen donors and one chloride anion,

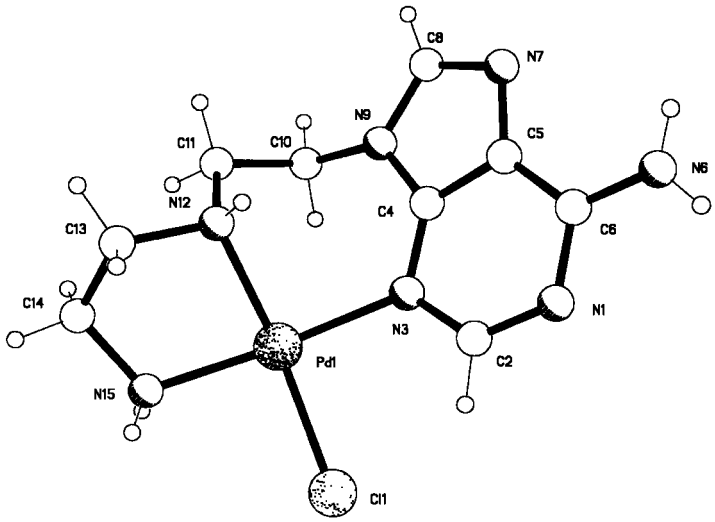

Figure 1. Molecular structure of the cation **1**, $[PdCl(A\text{-}N3\text{-Et-en})]^+$, featuring five- and seven-membered chelate rings. Selected bond lengths [Å]: Pd1–Cl1 2.3189(9), Pd1–N3 2.047(3), Pd1–N12 2.040(3), Pd1–N15 2.031(3); Pd1···H10A 2.851 Å.

adopts a distorted square-planar geometry. The ethylenediamine group and N3 of the adenine moiety contribute the three nitrogen donor atoms and hence the nucleobase–diamines act as tridentate ligands in each case. This gives rise to five- and seven-membered chelate rings in **1** and five- and eight-membered chelate rings in **2**. The co-ordination mode seen in these complexes is analogous to the macrochelation reported for nucleotides by Sigel et al.[6] The adenine moieties lie at angles of 40.1° and 72.9° with respect to the metal coordination plane for **1** and **2**, respectively. This latter value is close to that observed in [6,′6′,9-TMA-*N3*-Pd(dien)]$^{2+}$ (78.2°) (where TMA is 6′,6′,9-trimethyladenine)[7] suggesting that the propyl chain is of sufficient length to allow coordination at N3 without imposing additional geometric constraints.

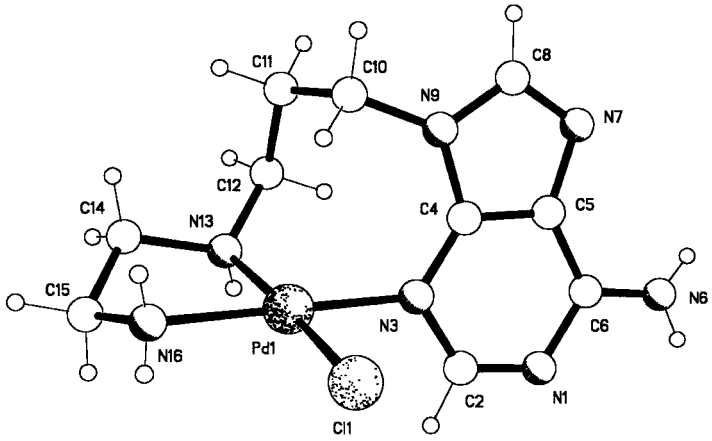

Figure 2. Molecular structure of the cation **2**, $[PdCl(A\text{-}N3\text{-Prop-en})]^+$, featuring five- and eight-membered chelate rings. Selected bond lengths [Å]: Pd1–Cl1 2.3000(10), Pd1–N3 2.031(3), Pd1–N13 2.045(3), Pd1–N16 2.010(3); Pd···H10A 2.521 Å.

In both complexes **1** and **2**, a consequence of the ligand-binding mode is to position one of the N9-bound methylene protons in close proximity to the metal centre and may be considered an agostic interaction (**1**: Pd···H 2.851 Å; H10A···Pd–N12 66°, H10A···Pd–Cl 122.6°; **2**: Pd···H 2.521 Å; H10B···Pd–N13 80.4°, H10B···Pd–Cl 99.3°). This structural feature accounts for the considerable downfield shift of the C10-bound proton resonances as observed by ^1H NMR spectroscopy. This may be attributed to the effect of the diamagnetic anisotropy of the pair of electrons in the Pd^{II} d_{z^2} orbital. Figure 3 compares the ^1H NMR spectrum of the ligand, A-Et-enH·Cl with that of the complex $[PdCl(A\text{-}N3\text{-Et-en})]BF_4$ in D_2O. The resonance corresponding to one of the protons bonded to C10 is clearly seen at $\delta = 5.60$ as compared to a chemical shift of $\delta = 4.25$ in the free ligand (the other proton is coincident with the solvent peak (HOD)). This feature appears to be diagnostic for N3 coordination, as similar effects have also been observed in N3-bound $[M(dien)]^{2+}$ (M = Pd, Pt) derivatives of 6′,6′,9-trimethyladenine.[7] Another noteworthy feature is the difference in chemical shifts of the resonances attributed to the aromatic protons H2 and H8 as compared to those in the spectrum of the free ligand.

While Pd^{II} may be considered typical in its reactivity with purine bases, that is the preferred binding sites are N1 and N7, there have been a number of recent reports of palladium co-ordinating to the less common site N3 of adenine derivatives. Steric hindrance of N1 and N7 has been used to promote such binding through the methylation of N6 in 6,6′,9-trimethyladenine.[7] Loeb and co-workers have designed a palladium-containing receptor which was found to bind adenine at N3 in conjunction with associated second-sphere π-stacking and

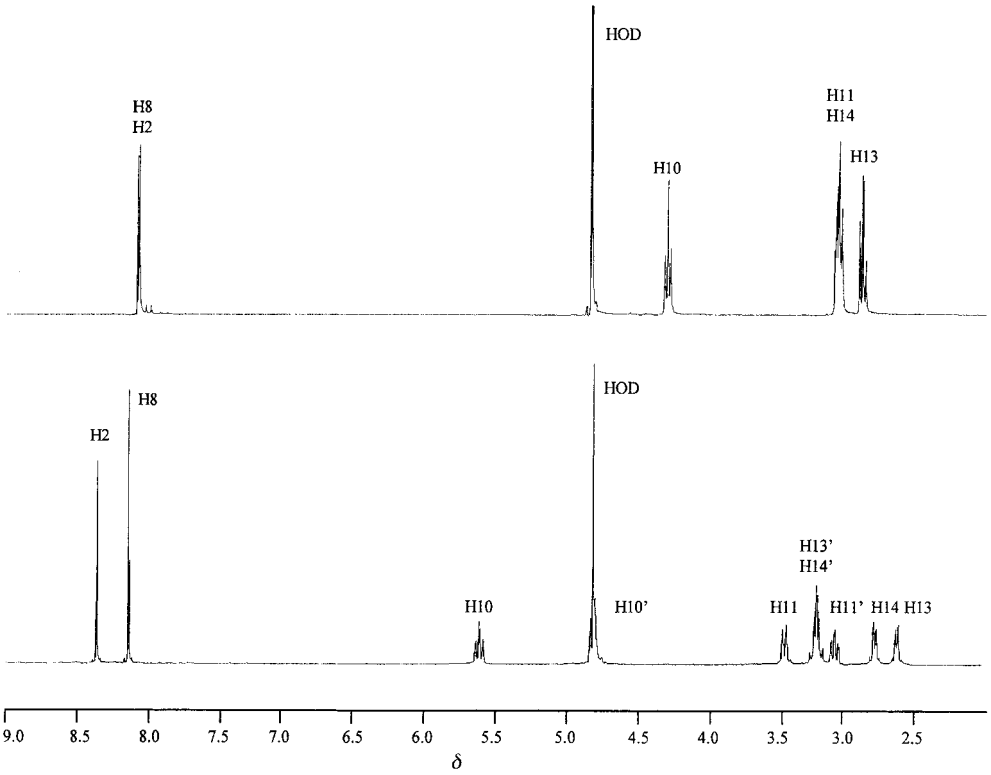

Figure 3. ^{1}H NMR spectra (500 MHz, D_2O) of A-Et-enH·Cl (top) and [PdCl(A-*N3*-Et-en)][BF_4] (bottom). Numbering used corresponds with the crystallographic scheme.

hydrogen bonding interactions.[8] A comparison of the interatomic distances in these compounds with those of **1** and **2** reveal no significant differences.

Analysis of the molecular packing in the crystal structures reveals in **1** intermolecular base-pairing interactions involving the Hoogsteen (H) faces of adjacent adenine moieties. An inversion-related pairing of H···H faces (N7···N6 distance 2.928 Å) generates an $R_2^2(10)$ motif[17] which further interacts with inversion-related neighbours through the WC-face N1 and the N15 amine proton (N1···N15 distance 2.971 Å) forming a centrosymmetric pattern (Figure 4). Together these form $R_2^2(10)$ $R_2^2(12)$chains which are crosslinked through Cl1···HN12 interactions (3.205 Å) to form sheets.

Figure 4. Intermolecular hydrogen bonding interactions in **1** generating an $R_2^2(10)$ $R_2^2(12)$ chain involving the W–C and H faces of the adenine moieties. These are crosslinked into sheets through NH···Cl interactions.

In **2** inversion-related pairs of molecules interact through the W–C face to form $R_2^2(8)$ rings (N1···N6 3.089 Å). Further interactions take place between each molecule in the pair with those in an adjacent pair through the metal-bound chloride ion and the second proton on N6 (N6···Cl1 3.439 Å). This interaction forms an $R_2^2(16)$ motif which contains parallel non-eclipsed adenine groups separated by about 3.5 Å (Figure 5).

Figure 5. Hydrogen-bonded inter-nucleobase interactions in **2**. Molecules related by inversion centre forming an $R_2^2(8)$ motif with the W–C faces of adenine.

Reactions of Pd^{II} and guanine derivatives: From the reaction of G-Et-enH·Cl with [$PdCl_2(MeCN)_2$] in MeCN/H_2O, after work-up and metathesis with $NaBF_4$, a sample was isolated which was characterised by single-crystal X-ray analysis as [PdCl(G-*C8*-Et-en)][BF_4], [**3**][BF_4]. This species again con-

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tains the ligand in a tridentate binding mode, but in this instance the binding site to the nucleobase is at C8.

The molecular structure of **3** is shown in Figure 6 and highlights the distorted square-planar geometry of the Pd^{II}

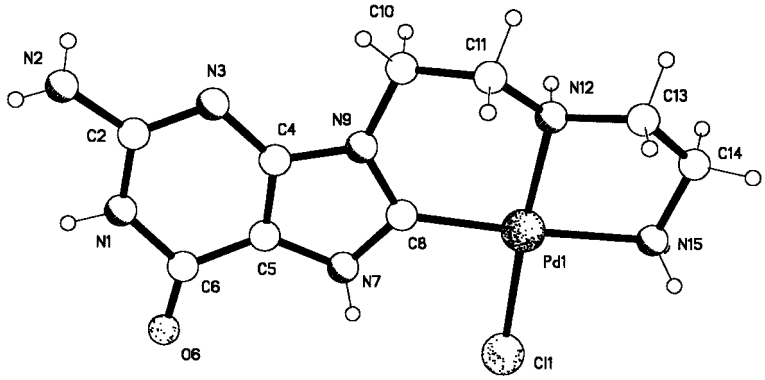

Figure 6. Molecular structure of the cation **3** [PdCl(G-*C8*-Et-en)]$^+$, featuring five- and six-membered chelate rings. Selected bond lengths [Å]: Pd1–Cl1 2.3084(9), Pd1–C8 1.974(3), Pd1–N12 2.038(3), Pd1–N15 2.094(3).

Figure 7 shows the intermolecular hydrogen bonding in **3** involving the self-complementary pairing of the minor groove edge of guaninyl moiety over an inversion centre (N3···N2 3.115 Å). This pairing is seen in a number of guanine-derived compounds including the complex *trans*-[Pt$(NH_3)_2$(6,6′,9-trimethylAde-*N3*)((EtGua-*N7*)]$^{2+}$.[23] Further hydrogen bonding in **3** occurs between the W–C face and the BF_4^- ion and the modified H face interacts strongly with occluded water (N7···O1 2.805 Å; O6···O1 2.781 Å).

In fact, reaction mixtures of [$PdCl_2(MeCN)_2$] and G-Et-enH·Cl were shown to contain several other species. ^{1}H NMR spectra indicated a mixture of at least three species, based upon the number of H8 resonances, in addition to the C8-metallated derivative **3**. The major one of these three had spectral features which were indicative of N3 coordination (multiplets at $\delta = 6.06$ and 4.93 in D_2O, for the protons attached to methylene group adjacent to N9). ES-MS data on reaction mixtures revealed the presence of a dimer, *m/z* 685 corresponding to [$Pd_2L_2 - 3H$]$^+$ as well as the major peaks at *m/z* 380 and 342 for complexed ions [PdLCl]$^+$ and [PdL – H]$^+$. We have previously characterised dimeric complexes such as [Zn_2(G-Prop-en)Cl_2] which involves N7 binding to one metal ion, while the diamine function binds a second.[24] Analogous species can easily be envisaged with Pd^{II} ions. However, attempts to isolate these minor species from the reaction mixtures were unsuccessful.

It was similarly the case with the G-Pr-enH.Cl ligand that analysis of reactions with Pd ions revealed the formation of multiple species and isolation of pure compounds was problematic. For instance, ^{1}H NMR spectroscopy of the reaction mixtures of [$PdCl_2(MeCN)_2$] and G-Pr-enH·Cl contained five distinct resonances corresponding to G-H8

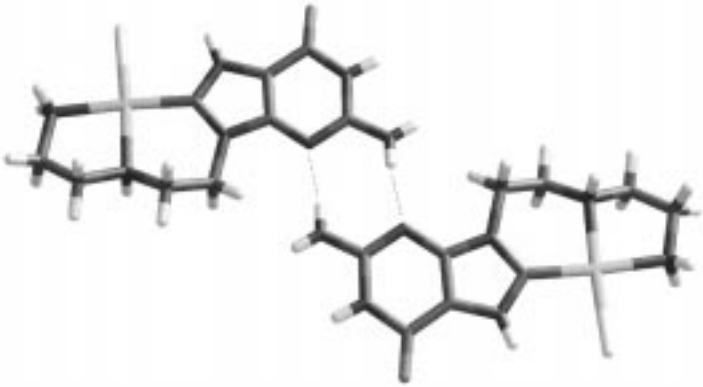

Figure 7. Inter-nucleobase interactions in [**3**][BF_4] involving the minor-groove edge of the guanine moieties forming $R_2^2(8)$ motif. The N2···N3 separation is 3.115 Å.

formed by co-ordination of the en group, a chloride anion and the C8 of the guanine moiety. The complex cation **3** is virtually planar (mean deviation from Pd1/Cl1-C8-N12-N15 plane = 0.8977 Å), though the two ethylene chains are disordered over two positions. The Pd–$C8_{gua}$ bond length is 1.974(3) Å in **3** and compares with 1.989(3) Å for Ru–$C8_{ade}$ in [Ru(Cl_2dmso-(A-*C8*-Et-en)][12b] and with distances of 1.943 Å and 2.040 Å for palladium imidazolin-2-ylidene complexes.[18] Metallation at C8 is accompanied by proton transfer to N7 which is indicated by the downfield resonance at $\delta = 11.57$ in the ^{1}H NMR spectrum.

Examples of organometallic nucleobase derivatives that contain biomolecular metal–carbon bonds are limited, especially so for purines. Taube and Clark have reported on reactions of Ru^{II}/Ru^{III} ammines with a series of alkylated xanthine derivatives and observed C8-binding in several cases; however, the nucleobases adenine and guanine did not feature in these studies.[19] C8-mercurated guanine and inosine derivatives have been prepared, but these are poly-substituted with binding at C8 attributed to the increase in acidity of the C8 proton as a result of N7 coordination.[14] A similar argument has been put forward to account for the formation of *trans*-[Pd(8-(methylthio)theophyllinato-*N7*)-(theophyllinato-*C8*)(PPh_3)$_2$].[20]

Simple electron counting indicates that the guaninyl residue in **3** must act as a one-electron donor for the compound to be a 16-electron species.[21] In fact, **3** may be considered as a typical cyclometallation product, well known for Pd^{II} chemistry and generally considered to involve pre-coordination of an adjacent ligand followed by electrophilic substitution, in this case base-assisted by N7.[22] To our knowledge **3** represents the first structurally characterised example of a guanine residue to contain a metal-carbon bond. The complex is however analogous to the previously described adenine complex [$RuCl_2$dmso(A-*C8*-Et-en)] for which we were also able to isolate the pre-co-ordinated intermediate which bears a pendant adenine group.[12b]

($\delta = 7.70$, 7.85, 8.15, 8.23 and 8.24) with the resonance at $\delta =$ 8.15 most prominant. Positive ion ES-MS indicated the presence of oligomers with peaks at *m/z* 815 and 709 corresponding to $[Pd_3(G\text{-}Prop\text{-}en)_2\text{-}5H]^+$ and $[Pd_2(G\text{-}Prop\text{-}en)_2\text{-}3H]^+$ in addition to those at *m/z* 394 and 356 for mononuclear complexed ions $[PdCl(G\text{-}Prop\text{-}en)]^+$ and $[Pd(G\text{-}Prop\text{-}en) - H]^+$. Unfortunately, repeated attempts to isolate pure compounds by recrystallization from aqueous solutions were unsuccessful.

Single crystals of **4** which were suitable for crystallographic analysis were finally obtained in low yield (ca. 5%) by crystallization of the material obtained from reactions of G-Pr-enH·Cl with $PdCl_2$ in aqueous MeCN after halide metathesis with $AgNO_3$. ES-MS data for the crystalline material dissolved in aqueous solution contained peaks at *m/z* 356 and 709 which are assigned to $[Pd(G\text{-}Pr\text{-}en) - H]^+$ and $[Pd_2(G\text{-}Pr\text{-}en)_2\text{-}3H]^+$, respectively. Higher molecular weight species were not apparent.

In fact in the solid state, **4** was shown to contain a tetrameric assembly involving a ligand binding mode analogous to that seen in **1** and **2**, that is the diamine function and N3 of the nucleobase bind in a tridentate manner (Figure 8). However,

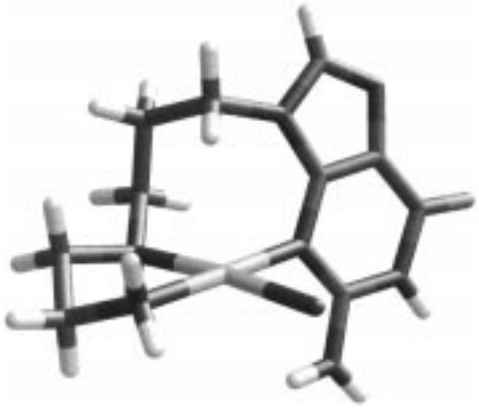

Figure 8. Mononuclear fragment of the $[Pd_4\text{-}G_4]$ quartet **4** highlighting the N3 co-ordination of the nucleobase and the similarity to **2**. Atomic numbering is conventional for the guanine residue and the alkyldiamine tether is as for **2**.

in addition guanine co-ordinates a second metal ion at N7 and this bridging mode assembles four $[Pd(G\text{-}N3\text{-}Pr\text{-}en)]^{2+}$ units into a tetrameric octa-cationic macromolecule (Figure 9). Each of the mononuclear *N7-N3*-co-ordinated guaninyl fragments bear, perhaps unsurprisingly, a striking resemblance to the *N3*-adeninyl complex **2** (compare Figure 8 with Figure 2). For example, in **4** the nucleobase lies at an angle of 72.2° to the and the short H10···Pd distance is 2.436 Å compared with 72.9° and 2.521 Å for these same parameters in **2**. To the best of our knowledge, **4** is only the second structurally characterised example of an N3-co-ordinated guanine derivative, the tri-platinum complex $[9\text{-}EtG(N1,N7,N3\text{-}Pt(NH_3)_3]$ being reported some time previously by Lippert et al.[25]

Figure 9 shows a view of the octacationic tetrameric unit. All the atoms in the tetramer occupy general positions in the crystal lattice, hence there is no crystallographic symmetry

Figure 9. Octacationic Pd-based guaninyl quartet, **4**, comprising $[Pd(G\text{-}N3,N7\text{-}Prop\text{-}en)]^{2+}$ moities. Selected structural parameters [Å]: Pd1–N7C 2.033, Pd2–N7 2.042, Pd3–N7A 2.038, Pd4–N7B 2.029, Pd–$N7_{av}$ 2.036; Pd1–N3 2.049, Pd2–N3A 2.081, Pd3–N3B 2.056, Pd4–N3C 2.049 Pd–$N3_{av}$ 2.059; Pd–$N13_{av}$ 2.043; Pd–$N16_{av}$ 2.016; Pd1···$Pd2_{edge}$ 7.243, Pd1···$Pd4_{edge}$ 7.237, Pd2···$Pd3_{edge}$ 7.269, Pd3···$Pd4_{edge}$ 7.244; Pd1···$Pd3_{diag}$ 9.871, Pd2···$Pd4_{diag}$ 10.062 Å.

element defining the square. The Pd···Pd edge distances exhibit a narrow range; Pd1···Pd2 7.243, Pd2···Pd3 7.269, Pd3···Pd4 7.244 and Pd1···Pd4 7.237 Å. The diagonal distances are Pd1···Pd3 9.871 and Pd2···Pd4 10.062 Å. The four Pd ions lie in a plane (mean deviation 0.8467 Å) with diagonally related ions exhibiting deviation in the same direction (Pd1 and Pd3 +0.85; Pd2 and Pd4 −0.85 Å). The guaninyl residues are inclined at about 52° to the plane defined by the four metal ions and alternate, as indicated by the W–C face of the nucleobase, in an head-tail-head-tail manner around the square. Guaninyl groups oriented in the same sense are inclined at angles of 65.4° and 66.0° relative to each other and the N1···N1B closest approach is 3.863 Å. Unusually for nucleobase-metal ion bridging modes it is the co-ordination geometry of the metal ion that generates the right angles of the assembly; N7C-Pd1-N3 90.2, N7-Pd1-N3A 90.2, N7A-Pd1-N3B 91.0, N7B-Pd1-N3C 90.5. The guaninyl residues in **4** act to form approximately linear bridges by co-ordinating at N3 and N7. More typical are 90° bridges formed through purine (N1 + N7) and 120° bridges through pyrimidine (N1 + N3) binding modes.[26]

Nucleobase quartets are an increasingly understood aspect of DNA chemistry and in addition to natural systems[27] a number of synthetic examples have been characterised.[28,29] A feature general to all these assemblies is a dependence on metal ions for formation, though the details of the metal ion···nucleobase interactions vary considerably. Interestingly, an alternative Pd-bridged guanine tetrameric structure has been proposed for solutions containing equimolar equivalents of $[Pd(en)(NO_3)_2]$ and 5′-GMP or 5′-IMP.[30] This complex has C_4 symmetry and involves metal ion binding at N1 and N7 (Figure 10).

Compound **4** is in fact the second example of a G-quartet generated through co-ordinate bond formation with these

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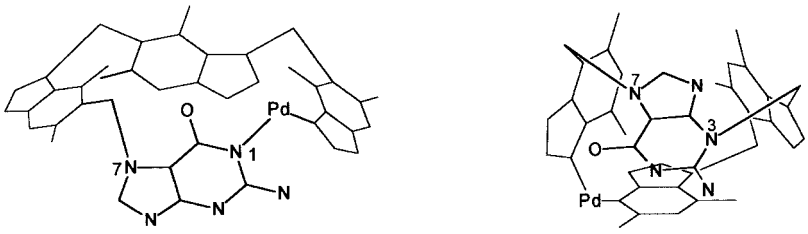

Figure 10. Proposed structure for $[Pd(en)_4(5'GMP)_4]^{4+}$ involving N1 + N7 binding (ref. [30]) compared to the structure of **4**.

ligand systems. The other example is based upon octahedrally co-ordinated Cd^{II} ions.[24] In this case the metal ions are ligated by the diamine function, N7 of the guaninyl residue, and H_2O to form squares which are extended into columns through bridging SO_4^{2-} ions. The absence of metal ion binding at N3 has a profound effect upon the structure of the individual tetrameric units, as illustrated in Figure 11. For example, the four G-residues lie effectively in the plane with the W–C faces pointing outwards from the centre of the square and this facilitates the stacking of tetrads into columns. By contrast, the head-tail-head-tail orientation of the guaninyl moieties in **4** is required to allow Pd–N3 binding. The two quartets may be considered as open and closed counterparts with interconversion being dependent on a change in the ligand binding mode [N7] ⇄ [N7 + N3] (Figure 11). The resulting [N7 + N3]

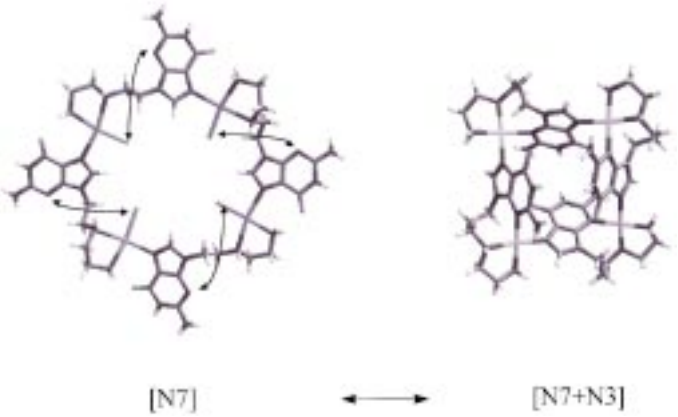

Figure 11. Comparison of the open and closed forms of $[Metal_4\text{-}G_4]$ quartets formed with guanine-alkyldiamines. Left, the open Cd-derived assembly which involves N7 binding and, right, the closed Pd-derived structure which involves N3 + N7. The arrows indicate the necessary ligand substitution for interconversion between the two forms.

mode seen in **4** hinders base ··· base stacking and in fact there are no inter-tetramer interactions in the crystal lattice of **4**. However, as with the $[Cd_4\text{-}G_4]$ tetrad, *the W–C faces of the guaninyl groups are available for hydrogen bonding interactions.* This common feature of the quartets generated through co-ordinate bond formation is in contrast to the majority of nucleobase quartets which are *assembled through complementary hydrogen bonding interactions.* Compound **4** along with the Cd-containing derivative reported elsewhere[24] collectively extend the range of nucleobase quartet architectures to include examples which retain a capacity for base pairing interactions.

Conclusion

The attachment of a chelating tether to the N9 position of the purine nucleobases, adenine and guanine, enables the preparation of novel nucleobase complexes. Moreover, the presence of the tethered group highlights some differences in the reactivities of the two bases. For instance, with palladium, cyclometallation may occur with guanine but under similar conditions this was not observed with adenine.

Furthermore, with guanine there is a greater tendency for polynuclear species to be isolated compared to adenine.[24] In fact, **3** is the only mononuclear complex containing guanine we have isolated to date. This may be rationalised from the known reactivity of the respective N7 site with G > A. This factor also accounts for the greater tendency for reactions with G ligands to give multiple species compared to those containing A.

Finally, metal ion binding at the purine N3 site in these diamine systems has generally been restricted to adenine.[12, 16, 24] However, guanine-N3 co-ordination has been demonstrated some time ago[25] and the palladium-G-quartet **4** extends this exclusive class of compounds. Furthermore this complex emphasises that the steric demand of the 2-amino group of guanine is not prohibitive to metal ion co-ordination at the minor groove N3 site.

Experimental Section

Materials: 9-(2-Chloroethyl)adenine and 9-(3-chloropropyl)adenine were prepared by a published procedure[31] and converted to the corresponding ethylenediamine by reaction with neat reagent as described previously.[12] 9-(2-Chloroethyl)guanine and 9-(3-chloropropyl)guanine were prepared following literature methods from amino-6-chloro-purine[32] and reacted in an analogous manner to the adenine derivatives to form the corresponding ethylenediamines as hydrochloride salts.[12b, 24]

NMR spectra were measured on a Joel Lambda 500 spectrometer. Mass spectra were measured at the EPSRC MS Service University of Wales, Swansea.

Preparation of [Pd(A-*N3*-Et-en)Cl]Cl, [1]Cl: $PdCl_2$ (0.50 g, 2.8 mmol) was dissolved in refluxing acetonitrile (80 mL). To this was added dropwise an aqueous solution (30 mL) of ethylenediamine-N,-9-ethyladenine hydrochloride (0.73 g, 2.8 mmol), the mixture was heated at reflux for 16 h. The solvent was removed from the cooled solution under reduced pressure and the resulting solid residue was dissolved in water (100 mL), any undissolved solids were removed by filtration. Evaporative removal of the solvent yielded the crude product which was recrystallised from a minimum volume of water to afford the product as a microcrystalline yellow powder (0.75 g, 67 %). ^{1}H NMR ([D$_6$]DMSO): $\delta = 2.45$ (m, 2H; H13′, H14), 2.85 (m, 1H; H11′), 2.95 (m, 1H; H14′), 3.00 (m, 1H; H13), 3.25 (m, 1H; H11), 4.71 (d, $J = 15$ Hz, 1H; H10′), 5.20 (ddd, $J = 4$, 12, 16, Hz, 1H; H10), 5.25 (m, 1H; H15/H15′), 5.40 (m, 1H; H15/15′), 7.00 (m, 1H; H12), 8.15 (s, 1H; H6/H6′), 8.25 (s, 1H; H8), 8.30 (s, 1H; H2), 8.43 (s, 1H; H6/6′): elemental analysis calcd (%) for $C_9H_{15}Cl_2N_7Pd \cdot 2H_2O$: C 24.87, H 4.40, N 22.56; found: C 24.27, H 4.24, N 21.46; MS: *m/z* (%): 364 $[M]^+$, 326 (100) $[M - HCl]^+$. The chloride salt was converted to the corresponding BF_4^- salt using a saturated aqueous solution of $NaBF_4$, to aid in the growth of single crystals suitable for X-ray diffraction studies.

[Pd(A-*N3*-Pr-en)Cl]Cl, [2]Cl: An aqueous solution (15 mL) of ethylenediamine-*N*-propyladenine hydrochloride (0.38 g, 1.4 mmol) was added dropwise to a refluxing solution of $PdCl_2$ (0.25 g, 1.4 mmol) in acetonitrile (40 mL). On the addition of the ligand solution a fine yellow solid precipitated. The mixture was allowed to continue at reflux for 16 h. The solid was collected from the cooled solution by filtration and washed with acetonitrile. The crude product was recrystallised from water (15 mL) to afford the product as a yellow microcrystalline solid (0.42 g, 73 %): ^{1}H NMR ([D$_6$]DMSO): $\delta = 1.88$ (m, 1H; H11′), 1.99 (m, 1H; H12′), 2.34 (m, 3H; H11, H12, H14), 2.44 (m, 1H; H15), 2.62 (m, 1H; H15′), 2.90 (ddd, $J = 4$, 12, 16 Hz, 1H; H14), 4.82 (dd, $J = 4$, 15 Hz, 1H; H10), 5.27 (d, $J = 7$ Hz, 1H; H16), 5.56 (m, 1H; H16′), 6.91 (m, 1H; H10′), 7.33 (d, $J = 9$ Hz, 1H; H13), 8.13, (s, 1H; H6/6′), 8.20 (s, 1H; H6/6′), 8.27 (s, 1H; H2), 8.34 (s, 1H; H8): elemental analysis calcd (%) for $C_{10}H_{17}Cl_2N_7Pd \cdot 2H_2O$: C 26.77, H 4.72, N 21.85; found: C 26.24; H, 4.44; N, 21.18; MS: *m/z* (%): 378 (100) $[M]^+$, 340 (100) $[M - HCl]^+$. Suitable crystals for single-crystal X-ray diffraction analysis were grown by the controlled cooling of a hot aqueous solution

[Pd(G-*C8*-Et-en)Cl]BF$_4$, [3]BF$_4$: To a refluxing solution of $PdCl_2$ (0.07 g, 0.4 mmol) in acetonitrile (30 mL) was added dropwise a solution of ethylenediamine-*N*,9-ethylguanine hydrochloride (0.11 g, 0.4 mmol) in water (25 mL). The mixture was stirred at reflux for 16 h. The solvent was removed from the cooled solution in vacuo. The solid residue was dissolved in a minimum volume of water (5 mL), the addition of a saturated aqueous solution of $NaBF_4$ afforded the crude product as an orange/brown solid, (0.07 g, 41 %). Crystalline material suitable for analysis by X-ray diffraction was obtained by the controlled cooling of a hot aqueous solution: ^{1}H NMR ([D$_6$]DMSO): $\delta = 2.44$ (m, 1H; H13), 2.58 (m, 1H; H14), 2.81 (m, 1H; H13), 3.11 (m, 1H; H14), 3.13 (m, 2H; H11, H11), 4.40 (m, 1H; H10), 4.49 (m, 1H; H10), 5.30 (s br, 1H; H15), 5.67 (s br, 1H; H15), 7.04 (m, 1H; H12), 7.13 (s, 1H; H2). 7.24 (s, 1H; H2), 10.93 (s (broad), 1H; H1), 11.51 (s br, 1H; H7): elemental analysis calcd (%) for $C_9H_{15}ClN_7OPdBF_4$: C 23.20; H 3.24; N 21.04; found: C 23.37; H 3.38; N 20.58; ES-MS: *m/z* (%): 380 (100) $[M]^+$ 342 (100) $[M - HCl]^+$.

Reaction of Pd^{II} with G-Pr-enH · Cl to give 4: $PdCl_2$ (0.19g, 1.04 mmol) was dissolved in refluxing acetonitrile (30 mL). After 1 h the solution was cooled to room temperature and $AgNO_3$ was added with stirring. Precipitated AgCl was removed by filtration through celite and the filtrate heated to reflux. To this was added dropwise an aqueous solution (30 mL) of ethylenediamine-*N*,9-propylguanine hydrochloride (0.30 g, 1.04 mmol). The mixture was refluxed for a further 3 h, the resulting yellow solution was concentrated under reduced pressure. On standing a yellow powder precipitated and was collected by filtration. The crude material was recrystallised from aqueous solution. ^{1}H NMR ([D$_6$]DMSO): $\delta = 1.99$ (m, 1H; H14), 2.11 (m, 2H; H14′, H11), 2.64 (m, 2H; H12, H15), 2.79 (m, 2H; H12′, H15′), 3.06 (m, 1H; H11′), 4.02 (m, 1H; H10), 4.18 (m, 1H; H10′), 5.28 (s, 1H; H16), 5.44 (s, 1H; H16′), 6.71 (s, 1H; H13), 6.96 (s, 2H; H2, H2′). 8.17 (s, 1H; H8), 11.22 (s, 1H; H1); elemental analysis calcd (%) for $[Pd_4(C_{40}H_{68}N_{28}O_4)Cl_4](NO_3)_4 \cdot 4HCl \cdot 4H_2O$: C 23.6, H 3.9, N 22.0; found: C 23.14, H 3.70, N 21.80. This indicates that the removal of Cl^- ions with $AgNO_3$ was imcomplete. A small quantity (ca. 5 %) of crystalline material (**4**) suitable for single-crystal X-ray diffraction analysis was obtained from a slowly evaporating aqueous solution.

X-ray diffraction studies

Crystal data for [1]BF$_4$: $C_9H_{15}ClN_7PdBF_4$, $M_r = 449.9$, triclinic, space group $P\bar{1}$, $a = 6.5449(11)$, $b = 10.0951(17)$, $c = 12.321(2)$ Å, $\alpha = 99.515(5)$, $\beta = 105.391(4)$, $\gamma = 105.649(4)^\circ$, $V = 730.8(2)$ Å^3, $Z = 2$, $\rho_{calcd} = 2.045$ g cm^{-3}; $Mo_{K\alpha}$ radiation, $\lambda = 0.71073$ Å, $\mu = 1.505$ mm^{-1}, $T = 160$ K. Of 4513 measured reflections, corrected for absorption, 3139 were unique ($R_{int} = 0.0638$, $\theta \leq 28.3^\circ$); $R = 0.0350$ (*F* values, $F^2 > 2\sigma$), $R_w = 0.0961$ (F^2 values, all data), GOF = 1.068 for 224 parameters, final difference map extremes +1.09 and −1.46 e Å^3. The structure was solved by direct methods. All non-H atoms were refined anisotropically. H atom coordinates were refined for N-H atoms with $U_{iso} = 1.2U_{eq}$ (N). For H atoms attached to carbon a riding model was used.

Crystal data for [2]Cl: $C_{10}H_{21}Cl_2N_7O_2Pd$, $M_r = 448.6$, triclinic, space group $P\bar{1}$, $a = 7.0346(8)$, $b = 7.3548$ (9), $c = 17.801(2)$ Å, $\alpha = 88.670(2)$, $\beta = 80.500(3)$, $\gamma = 64.645(2)^\circ$, $V = 819.69(17)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.818$ g cm^{-3}; synchrotron radiation, $\lambda = 0.6956$ Å, $\mu = 1.475$ mm^{-1}, $T = 160$ K. Of 4655 measured reflections, corrected for absorption, 2909 were unique ($R_{int} = 0.0265$, $\theta \leq 25.7^\circ$); $R = 0.0397$ (*F* values, $F^2 > 2\sigma$), $R_w = 0.1059$ (F^2 values, all data), GOF = 1.079 for 231 parameters, final difference map extremes +1.07 and −1.41 e Å^3. The structure was solved by direct methods. All non-H atoms were refined anisotropically. H atom coordinates were refined for N-*H* atoms with $U_{iso} = 1.2U_{eq}$ (N). For H atoms attached to carbon a riding model was used. The small crystal size ($0.20 \times 0.10 \times 0.01$ mm) necessitated data collection with synchrotron radiation, SRS at Daresbury Laboratory, station 9.8.

Crystal data for [3]BF$_4$ · 1.3 H$_2$O: $C_9H_{15}ClN_7OPdBF_4 \cdot 1.3H_2O$, $M_r = 489.9$, monoclinic, space group $P2_1/c$, $a = 12.5802(17)$, $b = 14.1472(19)$, $c = 9.4291(12)$ Å, $\beta = 105.194(4)^\circ$, $V = 1619.5(4)$ Å^3, $Z = 4$, $\rho_{calcd} = 2.009$ g cm^{-3}; $Mo_{K\alpha}$ radiation, $\lambda = 0.71073$ Å, $\mu = 1.378$ mm^{-1}, $T = 160$ K. Of 9849 measured reflections, corrected for absorption, 3695 were unique ($R_{int} = 0.0259$, $\theta \leq 28.4^\circ$); $R = 0.0341$ (*F* values, $F^2 > 2\sigma$), $R_w = 0.0816$ (F^2 values, all data), GOF = 1.027 for 268 parameters and 14 restraints. Final difference map extremes +0.86 and −0.77 e Å^3. The carbon atoms in the two ethylene chains were disordered over two sets of positions with major and minor sites occupied 63.2:36.8(7) %. The geometry and anisotropic displacement parameters were restrained in these parts of the molecule. The coordinates of H atoms on N2 and O(1W) were freely refined, all others were refined with a riding model as for **1**. H atoms were not located for the partially occupied water molecules of crystallization, O(2W). The structure was solved by direct methods.

Crystal data for 4: $C_{40}H_{88}Cl_2N_{34}O_{32}Pd_4$, $M_r = 2053.9$, monoclinic, space group $P2_1/c$, $a = 30.425(2)$, $b = 15.9284(12)$, $c = 16.5310(12)$ Å, $\beta = 105.714(2)^\circ$, $V = 7712.0(10)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.769$ g cm^{-3}; synchrotron radiation, $\lambda = 0.6942$ Å, $\mu = 1.090$ mm^{-1}, $T = 160$ K. Of 57349 measured reflections, corrected for absorption, 14546 were unique ($R_{int} = 0.1019$, $\theta \leq 25.0^\circ$); $R = 0.1167$ (*F* values, $F^2 > 2\sigma$), $R_w = 0.2570$ (F^2 values, all data), GOF = 1.207 for 1102 parameters and 806 restraints. Final difference map extremes +4.10 and −2.41 e Å^3. Two of the six nitrate ions are disordered. Of the ten water molecules one is split over two sites and a further two are at half occupancy. The structure was solved by direct methods. The crystal was extremely small ($0.07 \times 0.04 \times 0.01$ mm) and gave relatively poor data, even with intense synchrotron radiation.

Programs used: SHELXTL (G. M. Sheldrick, SHELXTL manual, Bruker AXS Inc., Madison, WI., USA, 1998, version 5.1). Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-102899 (**1**), CCDC-102900 (**2**), CCDC-147964 (**3**), CCDC-147965 (**4**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax:(+44) 1223-336-033; e-mail:deposit@ccdc.cam.ac.uk).

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